

Figure 1A: Duplex forming oligonucleotide constructs that utilize palindrome or repeat sequences

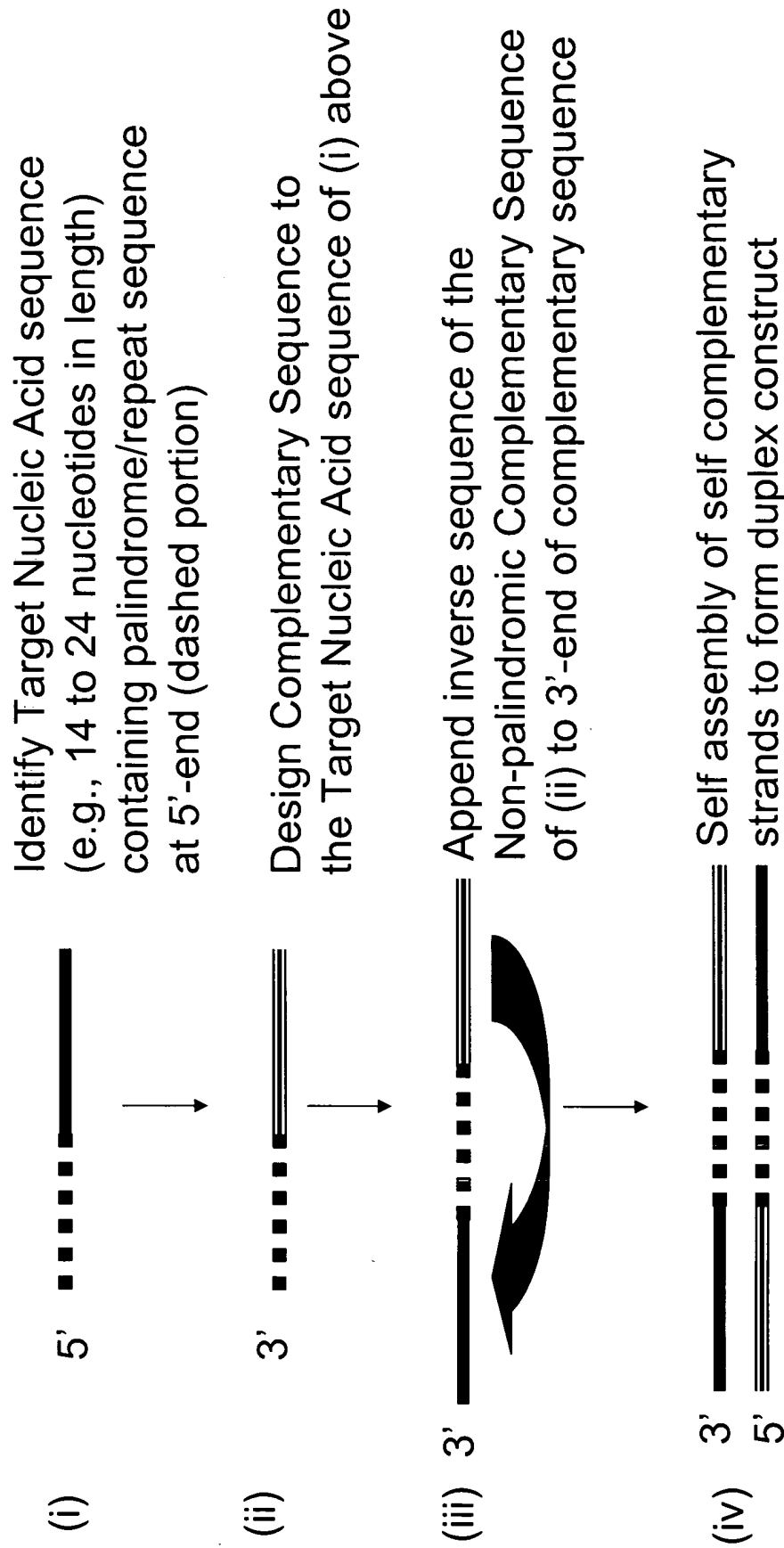


Figure 1B: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence

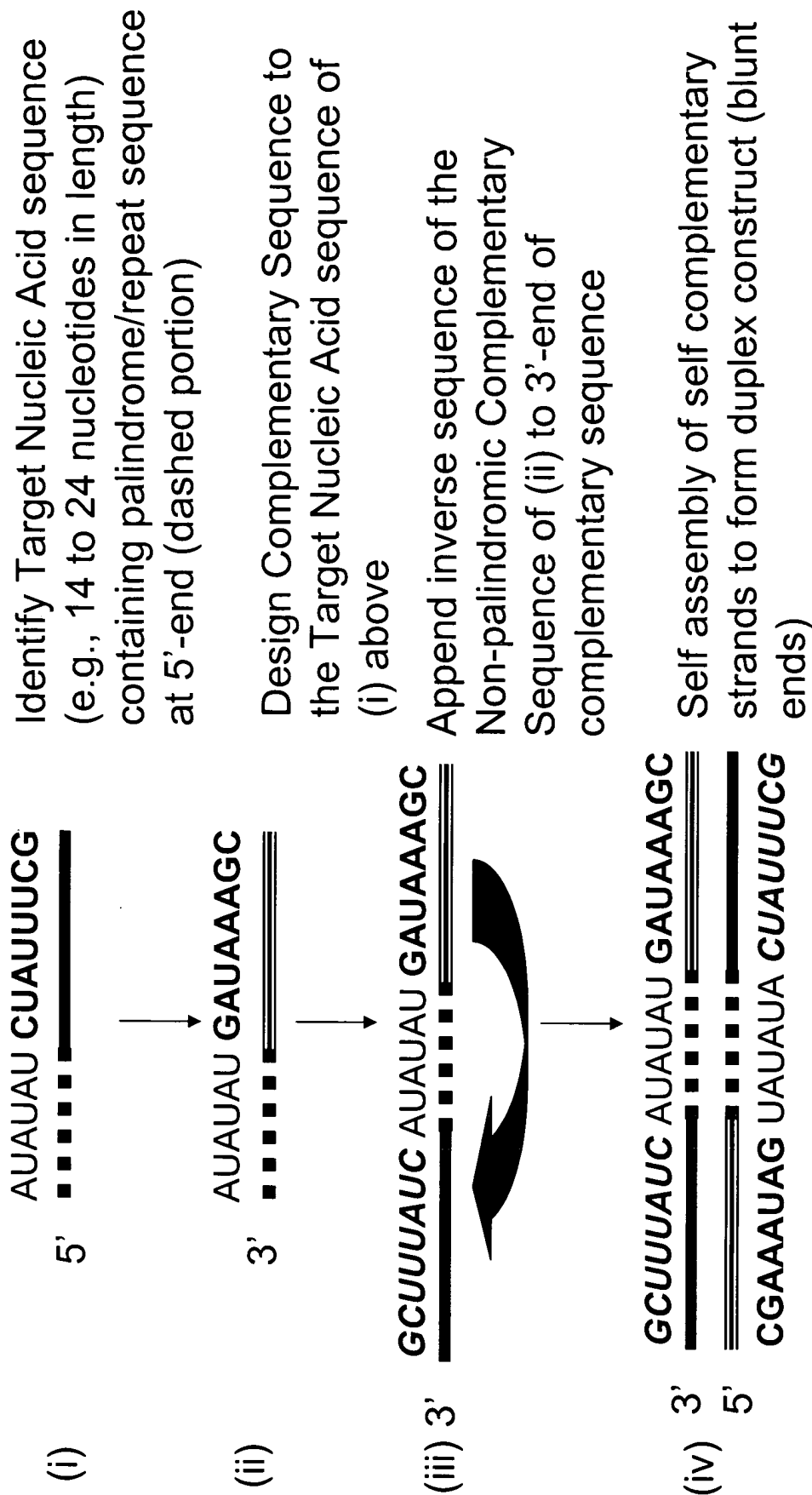


Figure 1D: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence, self assembly and inhibition of Target Sequence Expression

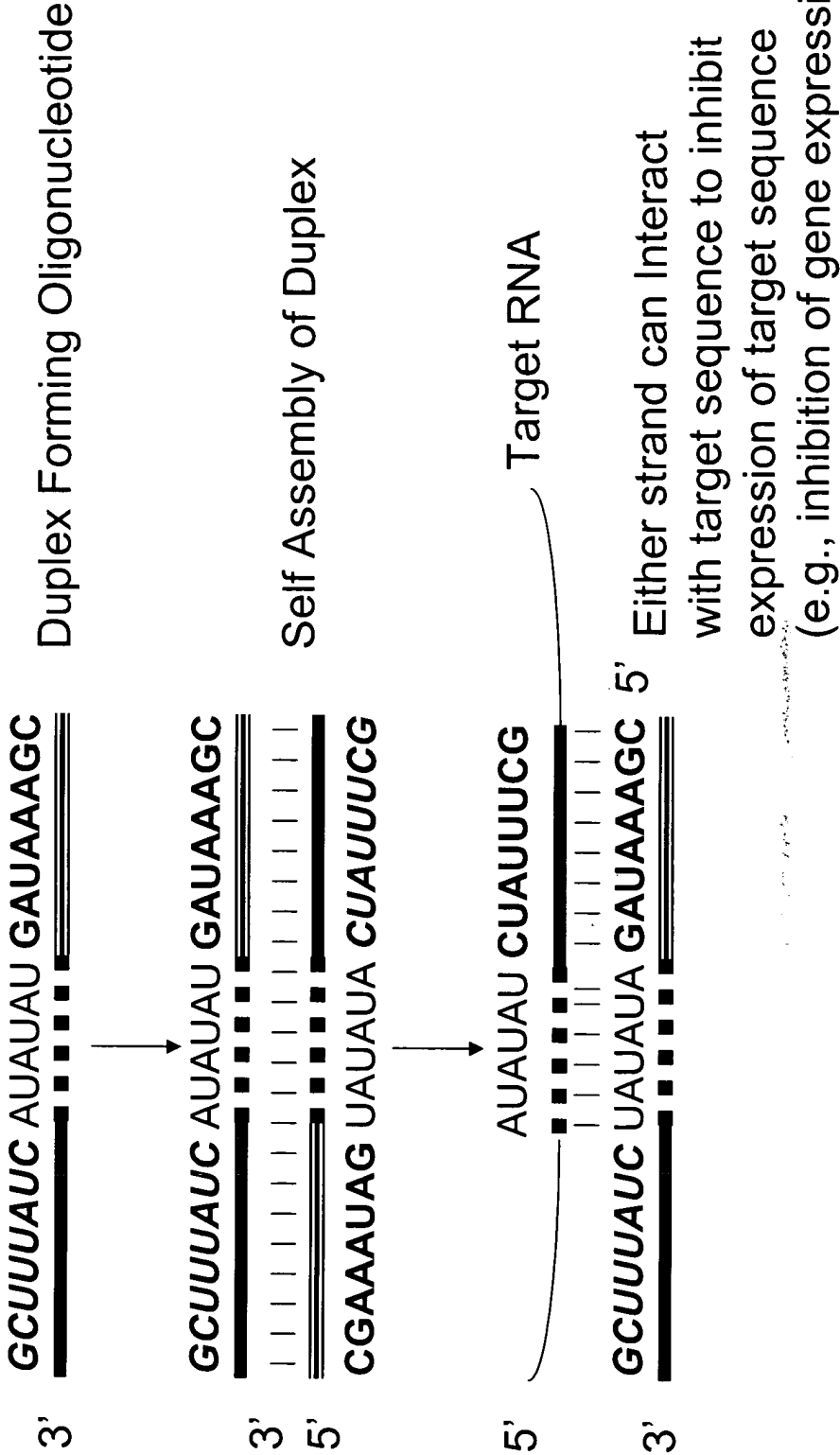


Figure 2: Duplex forming oligonucleotide constructs that utilize artificial palindrome or repeat sequences

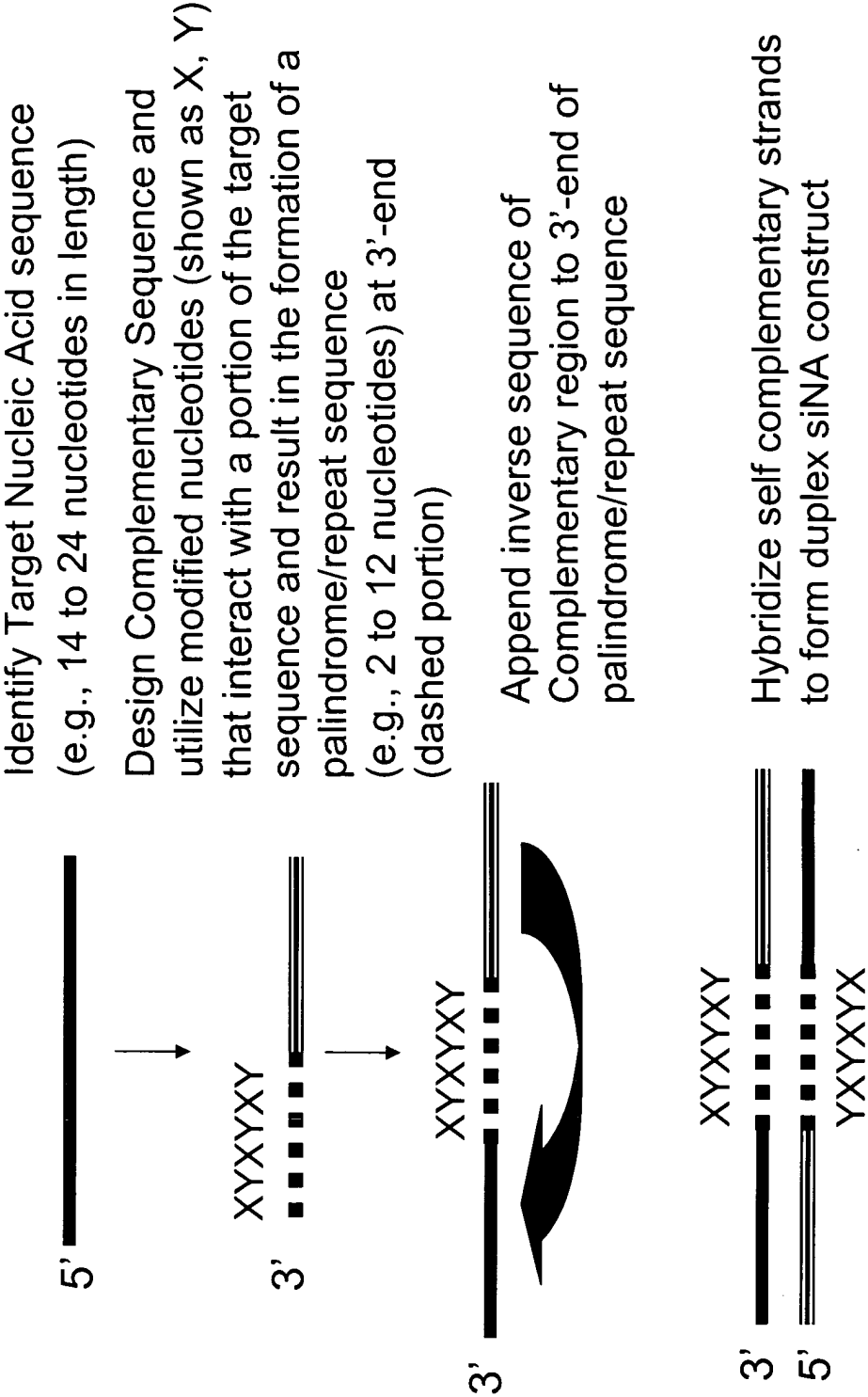
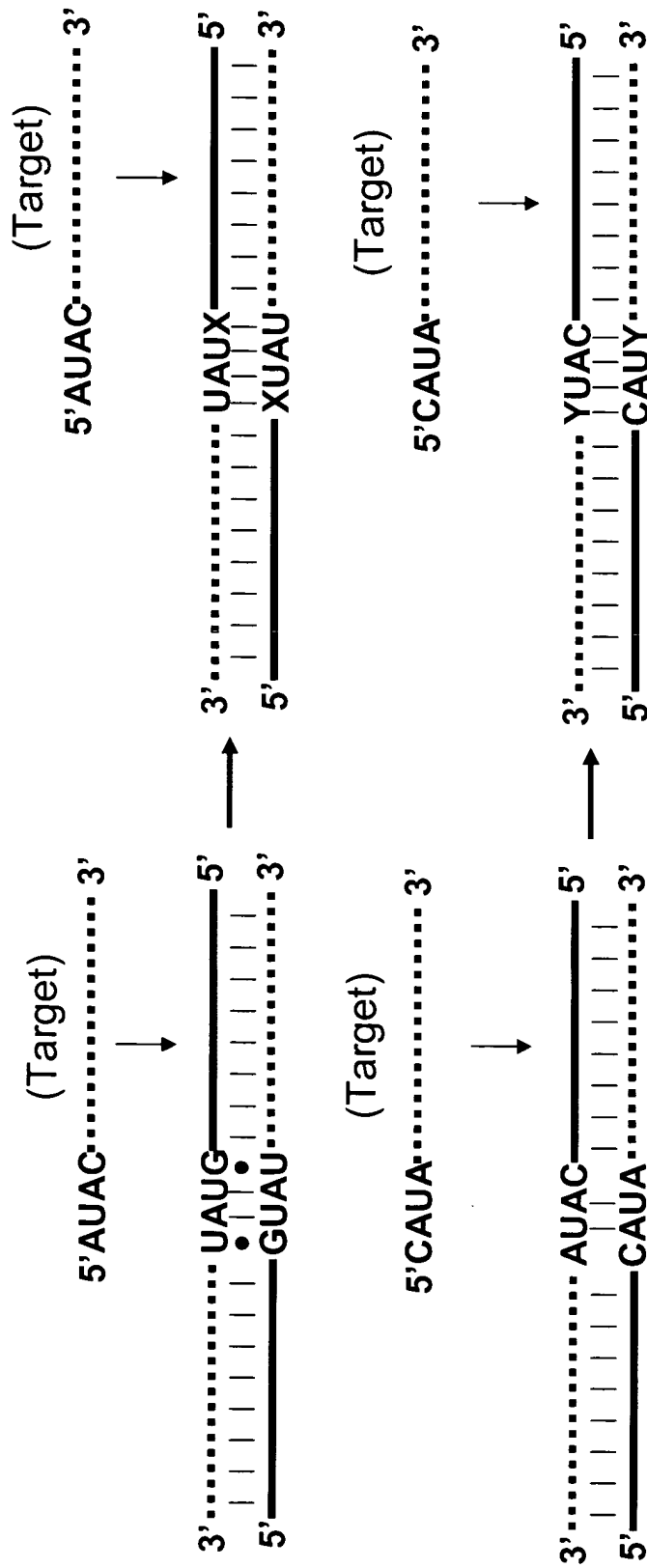


Figure 3: Examples of introducing artificial palindrome sequences in DFO constructs with a target nucleic acid not having a palindrome/repeat



X = 2-aminopurine

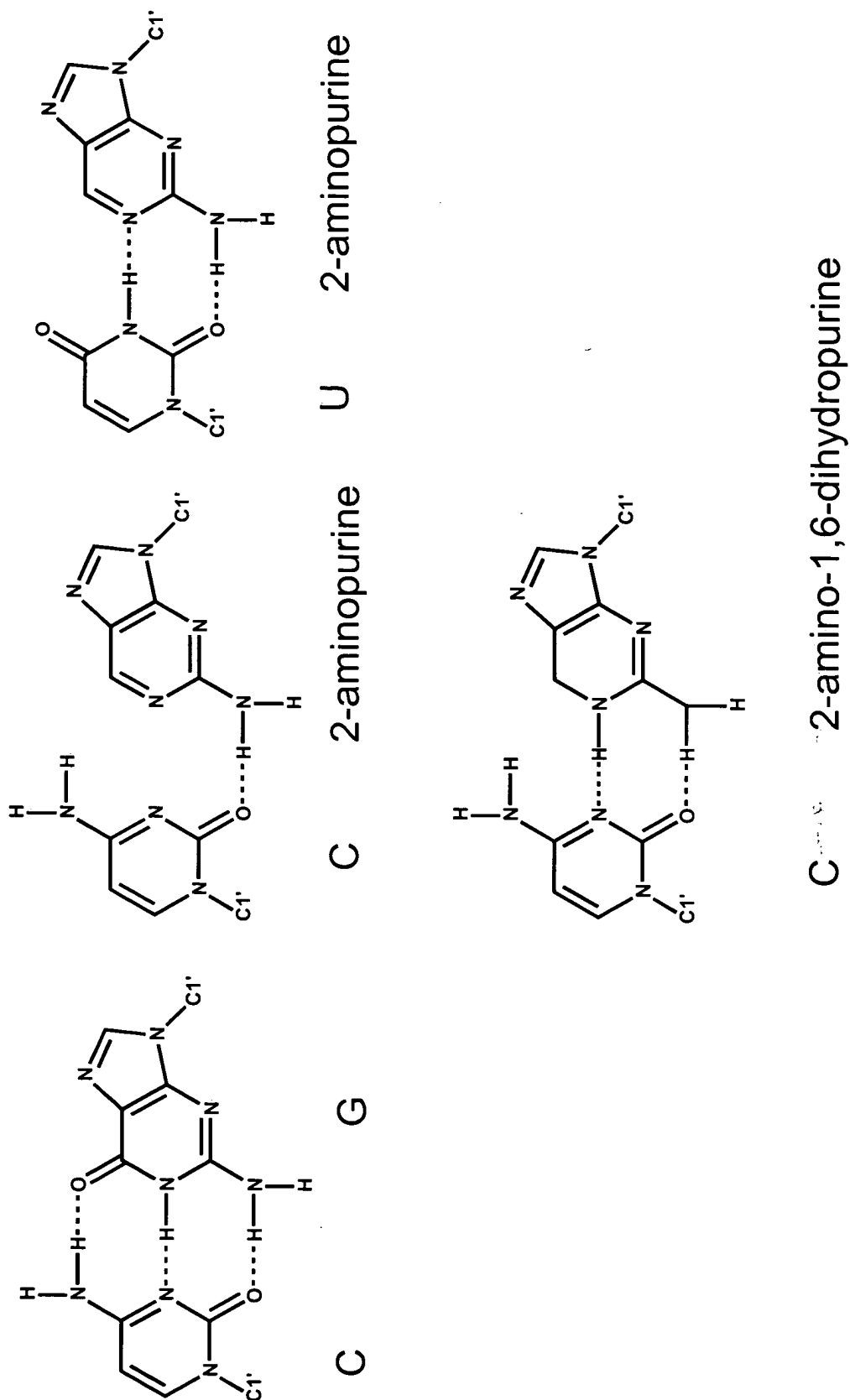
Y = 2-amino-1,6-dihydropurine

Similarly, other base modified pyrimidines can be utilized to make non-natural base pair with purines or vice versa

Figure 4: Examples of Palindromic (repeat) sites in mRNA targets

Examples: Palindromic restriction sites	Examples of sequences containing palindromic sites in HBV, HCV and VEGFR1
AAAUUU	HBV: These site are >90% conserves across subtypes
AAUU	UCCUAGGACCCUGCUCGU (SEQ ID NO: 1)
UUUAAA	GAGUCUAGACUCGUGGUGG (SEQ ID NO: 2)
UUAA	GUGCACUUCGCUUACCCUC (SEQ ID NO: 3)
AUAUAUA	HCV: These site are >90% conserves across subtypes
UAUAUAU	GCCAUGGCGUUAGUAUGAG (SEQ ID NO: 4)
GC GCGC	CUCCCGGAGAGCCAUAGU (SEQ ID NO: 5)
CGCGCG	ACCGGUGAGUACACCGGAA (SEQ ID NO: 6)
CCCGGG	CCCGGGAGGUCUCGUAGAC (SEQ ID NO: 7)
GGGCCC	
CCGG	VEGFR-1: human sequence
GGCC	UUUAAAAGGCACCCAGCAC (SEQ ID NO: 8)
ACAUGU	AUAUAUAUGAUAAAGCAUU (SEQ ID NO: 9)
CUCGAG	
GUGCAC	
AUAUGU (Wobble pair)	
ACAUAU (A-C mismatch)	

Figure 5: Examples of artificial palindromic sites generated using Modified nucleotides



Cytosine-2-amino-1,6-dihydropurine

Figure 6: Self-complementary DFO targeting VEGFR1 RNA

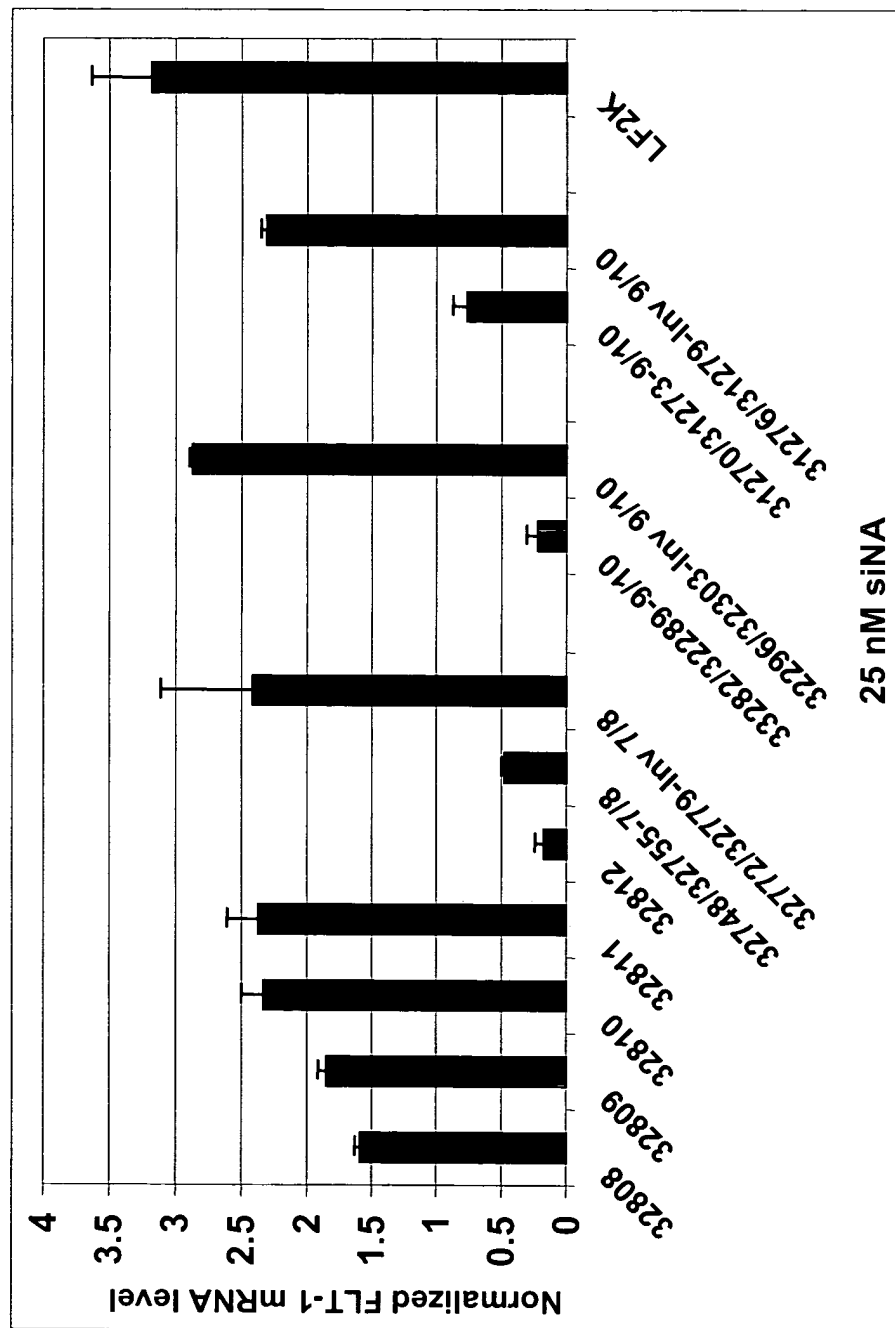


Figure 7: Self-complementary DFO targeting HBV RNA

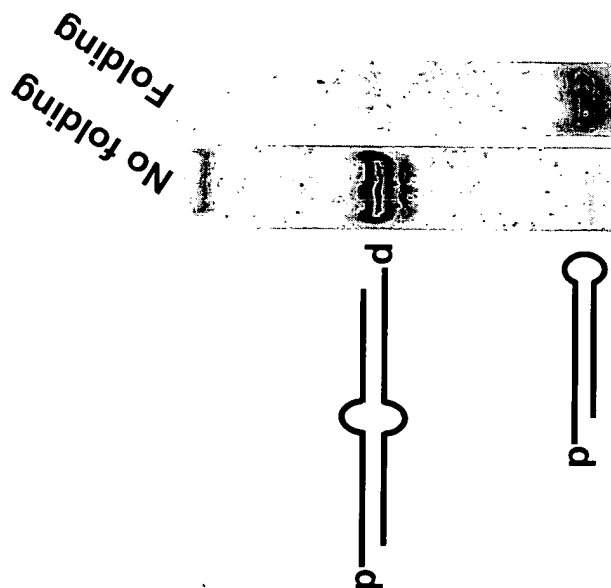
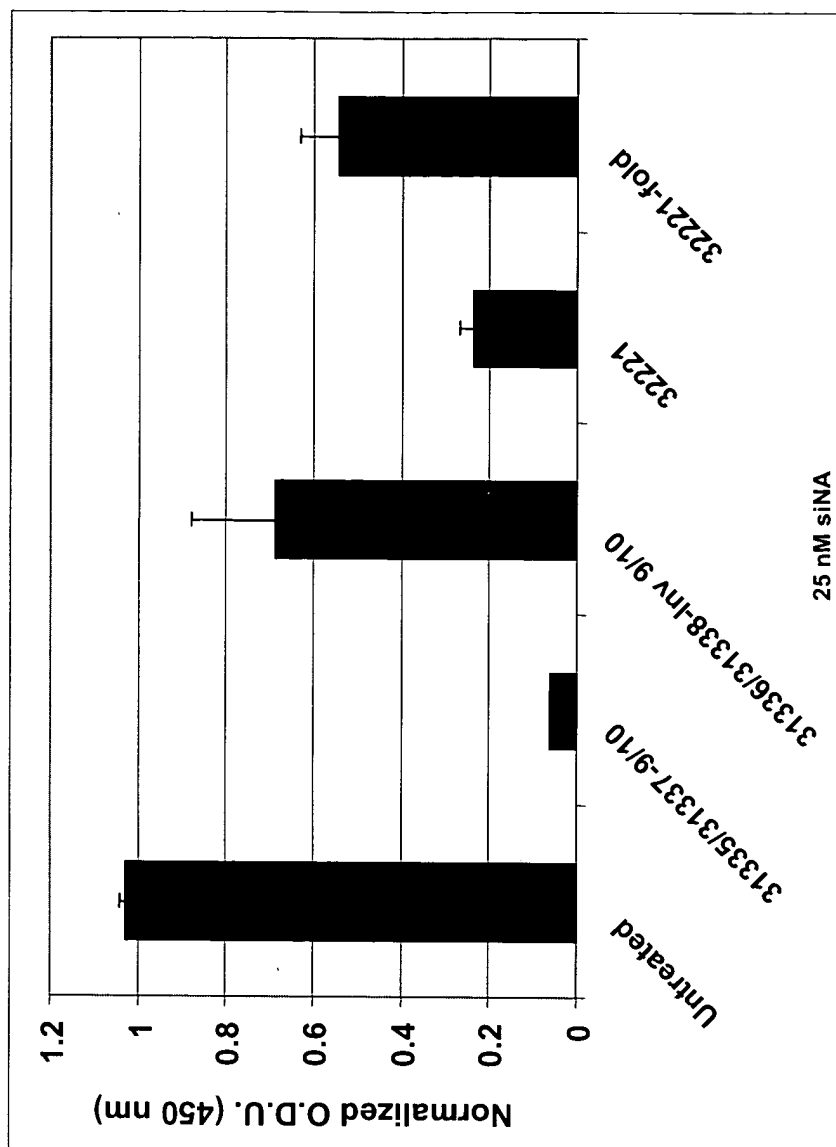
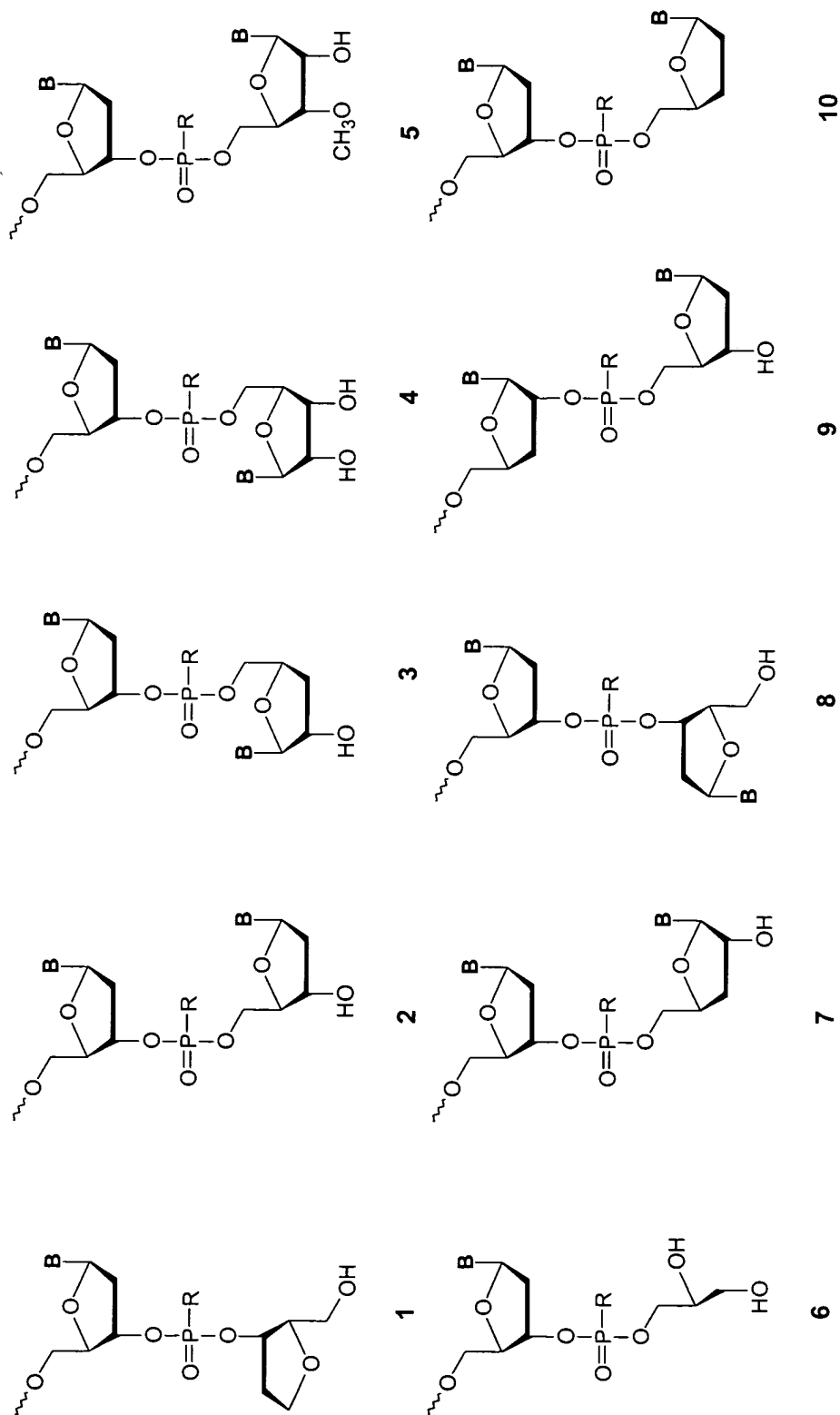
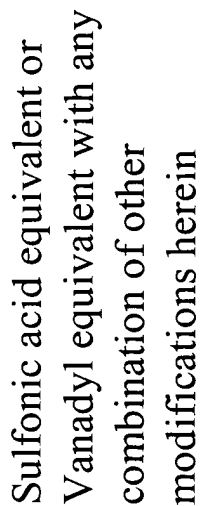


Figure 8



R = O, S, N, alkyl, substituted alkyl, O-alkyl, S-alkyl, alkaryl, or aralkyl
 B = Independently any nucleotide base, either naturally occurring or chemically modified, or optionally H (abasic).

Figure 9: 5'-phosphate modifications



A

5'-[R1] NNNNNNNNNNNNNNNNNNNNNN [R2] X X
 ←
 X X

↑
3'-EXTENSION

B

5'-[R1] NNNNNNNNNNNNNNNNNNNNNN [R2] X X
3'-[R1] NNNNNNNNNNNNNNNNNNNNNN [R2] X X

↑
CLEAVAGE WITH RESTRICTION ENZYMES 1 AND 2

C

5'-[] NNNNNNNNNNNNNNNNNNNNNN []
3'-[] NNNNNNNNNNNNNNNNNNNNNN []

↑
CLONE

U6 snRNA PROMOTER U6 snRNA PROMOTER

R1 = RESTRICTION SITE #1
R2 = RESTRICTION SITE #2
N = A, G, C, or T
X = A, G, C, or T

R1 = RESTRICTION SITE #1
R2 = RESTRICTION SITE #2
N = A, G, C, or T
X = A, G, C, or T